LETTER TO THE EDITOR (RESPONSE)

Development of a multi-organ rat model for evaluating chemopreventive agents: efficacy of indole-3-carbinol

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We appreciate the comments of Johnson and Huff. They focus their initial remarks on ‘Janus’ compounds that are carcinogenic. We wish to stress however, that there is no evidence that I3C is a complete carcinogen in any animal model. In that sense, I3C could be regarded as a potentially safer alternative to tamoxifen for intervention studies in high-risk patients. However, we have known for 15 years that I3C given post-initiation displays potent liver tumor promotional activity in the rainbow trout (1), which increases with dose and duration of exposure (2). The recent studies now extend this finding to the rat (3,4). Though I3C is often regarded as a natural anti-estrogen, there was ample evidence that this compound given orally can also elicit estrogenic responses in vivo, for instance in inducing estrogen-responsive genes in the trout (5) and in mimicking the ability of estradiol to suppress liver carcinogenesis in the mouse (6). It is this kind of dualistic activity, which Johnson and Huff so aptly term ‘Janus’ behavior, that raises our concern, especially for the general public consuming high doses of I3C as an ‘anti-estrogen’ supplement.

Current data does not support the clinical assumption that long-term I3C administration will have negligible risk. As a consequence, we believe it prudent at this time to restrict long-term clinical use of I3C to fully informed, high-risk individuals, for whom the potential therapeutic benefits may be judged to outweigh its potential risks in promoting liver cancer.

References


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